AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1-84 (Canceled)

85. (Currently Amended) A method of identifying ~~whether~~ a candidate compound ~~is~~ as a modulator of cardioprotection, comprising the steps of:

(a) contacting the candidate compound with a ~~GPCR~~ G protein-coupled receptor (GPCR), said receptor comprising an amino acid sequence selected from the group consisting of:

(i) the amino acid sequence of SEQ ID NO:2;

(ii) amino acids 2-433 of SEQ ID NO:2;

(iii) the amino acid sequence of SEQ ID NO:3;

(iv) amino acids 2-433 of SEQ ID NO:3;

(v) the amino acid sequence of a G protein-coupled receptor encoded by a polynucleotide that is amplifiable by polymerase chain reaction (PCR) on a human DNA sample using sequence specific primers SEQ ID NO:7 and SEQ ID NO:8; ~~and~~

(vi) the amino acid sequence of SEQ ID NO: 5;

(vii) the amino acid sequence of a G protein-coupled receptor encoded by a polynucleotide that hybridizes under stringent conditions to the complement of SEQ ID NO:1 or SEQ ID NO:4;

(viii) the amino acid sequence of a G protein-coupled receptor having an amino acid sequence having at least 90% identity to SEQ ID NO:2, SEQ ID NO:3, or SEQ ID NO:5; and

(ix) the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:3 wherein the phenylalanine at amino acid position 312 of SEQ ID NO:2 or SEQ ID NO:3 is substituted with lysine;

or a fragment or variant thereof, wherein the receptor couples to a G protein; and

(b) determining whether the receptor functionality is ~~modulated~~ inhibited or stimulated;

wherein ~~a change in~~ inhibition or stimulation of said receptor functionality is indicative of the candidate compound being a modulator of cardioprotection.

86. (Currently Amended) ~~A method of identifying whether a candidate compound is a modulator of a **RUP41** GPCR, said receptor comprising an amino acid sequence selected from the group consisting of:~~

~~(a) the amino acid sequence of SEQ ID NO:2;~~

~~(b) amino acids 2-433 of SEQ ID NO:2;~~

~~(c) the amino acid sequence of SEQ ID NO:3;~~

~~(d) amino acids 2-433 of SEQ ID NO:3;~~

~~(e) the amino acid sequence of a G protein-coupled receptor encoded by a polynucleotide that is amplifiable by polymerase chain reaction (PCR) on a human DNA sample using sequence specific primers SEQ ID NO:7 and SEQ ID NO:8;and~~

~~(f) the amino acid sequence of SEQ ID NO:5;~~

~~or a fragment or variant thereof, wherein the receptor couples to a G protein;~~

~~comprising the steps of:~~

~~(a') contacting the candidate compound with the receptor; and~~

~~(b') determining whether the receptor functionality is modulated;~~

~~wherein a change in receptor functionality is indicative of the candidate compound being a modulator of said GPCR~~ The method of claim 85, wherein the modulator of cardioprotection is a modulator of cardiomyocyte survival or cardiomyocyte apoptosis.

87. (Currently Amended) The method of claim 85 ~~claim 86~~, wherein the candidate compounds are screened as pharmaceutical agents for the prevention or treatment of a cardiovascular disorder, as pharmaceutical agents for the prevention or treatment of an ischemic heart disease, or as pharmaceutical agents for effecting a change in cardiovascular function.

88. (Currently Amended) A method of identifying ~~whether~~ a candidate compound ~~is~~ as an agonist of a **RUP41** GPCR ~~for use as~~ and a pharmaceutical agent for the prevention or treatment of a cardiovascular disorder~~,~~ or a pharmaceutical agent for the prevention or treatment of an ischemic heart

disease~~,~~ or a pharmaceutical agent for effecting a change in cardiovascular function, said receptor comprising an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:2;

(b) amino acids 2-433 of SEQ ID NO:2;

(c) the amino acid sequence of SEQ ID NO:3;

(d) amino acids 2-433 of SEQ ID NO:3;

(e) the amino acid sequence of a G protein-coupled receptor encoded by a polynucleotide that is amplifiable by polymerase chain reaction (PCR) on a human DNA sample using sequence specific primers SEQ ID NO:7 and SEQ ID NO:8; ~~and~~

(f) the amino acid sequence of SEQ ID NO:5;

(g) the amino acid sequence of a G protein-coupled receptor encoded by a polynucleotide that hybridizes under stringent conditions to the complement of SEQ ID NO:1 or SEQ ID NO:4;

(h) the amino acid sequence of a G protein-coupled receptor having an amino acid sequence having at least 90% identity to SEQ ID NO:2, SEQ ID NO:3, or SEQ ID NO:5; and

(i) the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:3 wherein the phenylalanine at amino acid position 312 of SEQ ID NO:2 or SEQ ID NO:3 is substituted with lysine;

or a fragment or variant thereof, wherein the receptor couples to a G protein; comprising the steps of:

(a') contacting the candidate compound with the receptor; and

(b') determining whether the receptor functionality is stimulated;

wherein stimulation of said receptor functionality is indicative of the candidate compound being an agonist of said GPCR ~~for use as~~ and a pharmaceutical agent for the prevention or treatment of a cardiovascular disorder~~,~~ or a pharmaceutical agent for the prevention or treatment of an ischemic heart disease~~,~~ or a pharmaceutical agent for effecting a change in cardiovascular function.

89. (Currently Amended) The method of claim 87 or claim 88 wherein the cardiovascular disorder is selected from the group consisting of:

(a) reduced cardiac output; and

(b) increased venous pressures.

90. (Currently Amended) The method of claim 87 or claim 88, wherein the ischemic heart disease is selected from the group consisting of:

(a) myocardial infarction;

(b) post-myocardial infarction remodeling; and

(c) congestive heart failure.

91. (Currently Amended) The method of claim 87 or claim 88, wherein the change in cardiovascular function is selected from the group consisting of:

(a) a decrease in cardiac hypertrophy;

(b) an increase in cardiac ejection volume;

(c) a decrease in ventricular chamber volume; and

(d) a decrease in cardiomyocyte apoptosis.

92. (Currently Amended) The method of claim 85 or 88, wherein said receptor is recombinant.

93. (Currently Amended) The method of claim 85 or 88, wherein said determining is through the measurement of the level of a second messenger selected from the group consisting of cyclic AMP (cAMP), cyclic GMP (cGMP), inositol triphosphate (IP_3), diacylglycerol (DAG) and Ca^{2+}.

94. (Previously Presented) The method of claim 93, wherein the intracellular level of cAMP is reduced.

95. (Currently Amended) The method of claim 85 or 88, wherein said determining is through the use of a Melanophore assay, through the measurement of GTPγS binding to a membrane comprising said GPCR, or through the use of a Gq(del)/Gi fusion construct assay.

96. (Currently Amended) The method of claim 85 or 88, further comprising the step of comparing the modulation of the receptor caused by the candidate compound to a second modulation of the receptor caused by contacting the receptor with a known modulator of the receptor.

97. (Previously Presented) A process for making a modulator of a RUP41 GPCR, comprising the steps of:

(a) identifying said modulator of the RUP41 GPCR; and

(b) synthesizing the modulator identified in (a).

98. (Previously Presented) A modulator identified according to a method of any one of claims 85 to 88.

99. (Previously Presented) The modulator of claim 98 wherein said modulator is selected from the group consisting of agonist, partial agonist, inverse agonist and antagonist.

100. (Previously Presented) The modulator of claim 98 wherein said modulator reduces the intracellular level of CAMP.

101. (Previously Presented) A method of modulating the activity of a RUP41 GPCR, said receptor comprising an amino acid sequence selected from the group consisting of

(a) the amino acid sequence of SEQ ID NO:2;

(b) amino acids 2-433 of SEQ ID NO:2;

(c) the amino acid sequence of SEQ ID NO:3;

(d) amino acids 2-433 of SEQ ID NO:3;

(e) the amino acid sequence of a G protein-coupled receptor encoded by a polynucleotide that is amplifiable by polymerase chain reaction (PCR) on a human DNA sample using sequence specific primers SEQ ID NO:7 and SEQ ID NO:8; and

(f) the amino acid sequence of SEQ ID NO:5;

or a fragment or variant thereof, wherein the receptor couples to a G protein, comprising the step of contacting the receptor with a modulator of claim 98.

102. (Previously Presented) The method of claim 101 wherein said contacting comprises administration of the modulator to a membrane comprising the receptor, to a cell or tissue comprising the receptor, or to an individual comprising the receptor.

103. (Previously Presented) A method of preparing a composition, comprising identifying a modulator of a RUP41 GPCR and then admixing a carrier and the modulator.

104. (Previously Presented) A pharmaceutical or physiologically acceptable composition comprising, consisting essentially of, or consisting of a modulator of claim 98.

105. (Previously Presented) A method of cardioprotection, of preventing or treating a cardiovascular disorder, of preventing or treating an ischemic heart disease, or of effecting a change in cardiovascular function comprising administering to an individual in need thereof said pharmaceutical or physiologically acceptable composition of claim 104.

106. (Previously Presented) The method of claim 105 wherein the cardiovascular disorder is selected from the group consisting of:

(a) reduced cardiac output; and

(b) increased venous pressures.

107. (Previously Presented) The method of claim 105 wherein the ischemic heart disease is selected from the group consisting of:

(a) myocardial infarction;

(b) post-myocardial infarction remodeling; and

(c) congestive heart failure.

108. (Previously Presented) The method of claim 105 wherein the change in cardiovascular function is selected from the group consisting of:

(a) a decrease in cardiac hypertrophy;

(b) an increase in cardiac ejection volume;

(c) a decrease in ventricular chamber volume; and

(d) a decrease in cardiomyocyte apoptosis.

109. (Previously Presented) The method of claim 105 wherein said individual is a mammal.

110. (Previously Presented) A method of making a knockout mouse or rat, wherein said knockout mouse or rat is predisposed to:

a cardiovascular disorder selected from the group consisting of reduced cardiac output and increased venous pressures; or

an ischemic heart disease selected from the group consisting of myocardial infarction, post-myocardial infarction remodeling and congestive heart failure;

comprising the step of knocking out a mouse gene encoding the polypeptide of SEQ ID NO:5, or knocking out a rat gene hybridizing at high stringency to the polynucleotide of SEQ ID NO:6.

111. (Currently Amended) The knockout mouse or rat made according to the method of claim 110.

112. (Previously Presented) A method of using the knockout mouse or rat of claim 111 to identify whether a candidate compound has therapeutic efficacy for the prevention or treatment of a cardiovascular disorder or an ischemic heart disease, comprising the step of administering or not administering the compound to the mouse or rat.

113. (Previously Presented) An isolated rat RUP41 polynucleotide selected from the group consisting of

(a) a polynucleotide comprising a contiguous span of at least 75 nucleotides of SEQ ID NO:6;

(b) a polynucleotide comprising a contiguous span of at least 150 nucleotides of SEQ ID NO:6:

(c) a polynucleotide comprising a contiguous span of at least 250 nucleotides of SEQ ID NO:6;

(d) a polynucleotide comprising a contiguous span of at least 350 nucleotides of SEQ ID NO:6; and

(e) a polynucleotide comprising a contiguous span of at least 500 nucleotides of SEQ ID NO:6; or the complement thereof

114. (Previously Presented) A recombinant vector, said recombinant vector comprising the isolated polynucleotide of claim 113.

115. (Previously Presented) A host cell comprising the recombinant vector of claim 114.

116. (Previously Presented) A GPCR Fusion Protein construct comprising a constitutively active G-protein coupled receptor and a G protein, said receptor comprising a RUP41 amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:2;

(b) amino acids 2-433 of SEQ ID NO:2;

(c) the amino acid sequence of SEQ ID NO:3;

(d) amino acids 2-433 of SEQ ID NO:3;

(e) the amino acid sequence of a G protein-coupled receptor encoded by a polynucleotide that is amplifiable by polymerase chain reaction (PCR) on a human DNA sample using sequence specific primers SEQ ID NO:7 and SEQ ID NO:8 and

(f) the amino acid sequence of SEQ ID NO:5;

or a fragment or variant thereof.

117. (Currently Amended) ~~A~~ The method of ~~identifying whether a candidate compound is a ligand of a RUP41 GPCR, said receptor comprising an amino acid sequence selected from the group consisting of:~~

~~(a) the amino acid sequence of SEQ ID NO:2;~~

~~(b) amino acids 2-433 of SEQ ID NO:2;~~

~~(c) the amino acid sequence of SEQ ID NO:3;~~

~~(d) amino acids 2-433 of SEQ ID NO:3;~~

~~(e) the amino acid sequence of a G protein coupled receptor encoded by a polynucleotide that is amplifiable by polymerase chain reaction PCR on a human DNA sample using sequence specific primers SEQ ID NO:7 and SEQ ID NO:8; and~~

~~(f) the amino acid sequence of SEQ ID NO:5;~~

~~or a fragment or variant thereof,~~ claim 85, wherein the modulator is a ligand, which is identified by a method comprising the steps of:

(a') contacting said receptor with an optionally ~~labled~~ labeled known ligand to the receptor in the presence or absence of said candidate compound;

(b') detecting the complex between said known ligand and said receptor; and

(c') determining whether less of said complex is formed in the presence of the candidate compound than in the absence of the candidate compound;

wherein said determination is indicative of the candidate compound being a ligand of said receptor.

118. (Previously Presented) A method of radioimaging, comprising providing or administering to an individual in need of said radioimaging a radiolabeled compound, wherein the compound is a modulator of a RUP41 GPCR or a ligand of a RUP41 GPCR.

119. (Previously Presented) The method of claim 118 for use in identifying an individual at risk for or progressing toward ischemic heart disease.

120. (Previously Presented) A non-human mammal transgenic for a human RUP41 GPCR, said receptor comprising an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:2;

(b) amino acids 2-433 of SEQ ID NO:2;

(c) the amino acid sequence of SEQ ID NO:2 wherein the phenylalanine at amino acid position 3 12 of SEQ ID NO:2 is substituted with lysine;

(d) the amino acid sequence of SEQ ID NO:3;

(e) amino acids 2-433 of SEQ ID NO:3;

(f) the amino acid sequence of SEQ ID NO:3 wherein the phenylalanine at amino acid position 312 of SEQ ID NO:3 is substituted with lysine; and

(g) the amino acid sequence of a G protein-coupled receptor encoded by a polynucleotide that is amplifiable by polymerase chain reaction (PCR) on a human DNA sample using sequence specific primers SEQ ID NO:7 and SEQ ID NO:8.

121. (Previously Presented) A method of using the transgenic non-human mammal of claim 120 to identify whether a compound has efficacy for cardioprotection, wherein the compound is a modulator of a RUP41 GPCR or a ligand of a RUP41 GPCR, said method comprising the step of administering the compound to the non-human mammal.

122. (New) The method of claim 85, further wherein stimulation of said receptor functionality is indicative of the candidate compound being a compound that increases cardioprotection.

123. (New) The method of claim 85 or 88 wherein said method comprises identifying an agonist of the GPCR.

124. (New) The method of claim 123, further comprising the step of formulating the agonist as a pharmaceutical.

125. (New) The method of claim 124, wherein the agonist is a partial agonist.

126. (New) The method of claim 85 wherein said method comprises identifying an inverse agonist or antagonist of the GPCR.

127. (New) The method of claim 126, further comprising the step of formulating the inverse agonist or antagonist as a pharmaceutical.

128. (New) The method of claim 124 or 127 wherein said contacting comprises contacting the candidate compound with a eukaryotic host cell comprising the GPCR or with membrane thereof that comprises the GPCR.

129. (New) The method of claim 128, wherein the eukaryotic host cell is a mammalian host cell.

130. (New) The method of claim 128, wherein the eukaryotic host cell is a melanophore host cell.

131. (New) The method of claim 128, wherein the eukaryotic host cell is a yeast host cell.